“Doing Double Duty”

Collecting Data for FDA and CMS in the Same Study

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Overview

- How FDA and CMS view evidence from clinical studies
- Practical considerations in leveraging a registration study to support CMS coverage and reimbursement determination

Data Opportunity

Conventional 510-K

Hybrid 510-K (with clinical data)

Pre-Market Approval (PMA)

Class III devices

"… support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury"

Perspectives – the Big Picture

- **FDA perspective**
  - *Regulatory approval to market*
  - safe?
  - effective?

- **CMS perspective**
  - *Coverage and reimbursement*
  - FDA approval?
  - Reasonable and necessary?
  - Medical benefit?

Point of Departure: Controlled Clinical Trial

- **Strengths**
  - Design features establish high *internal validity*
    - temporal sequence (intervention, outcomes)
    - causal relationship
    - non-spurious relationships
  - Execution helps ensure *credibility* of findings
    - protocol
    - monitoring
    - analysis
- **Weakness**
  - Lack of generalizability (?)
    - To different treatment settings
    - To different clinician
    - To different patient population

FDA vs. CMS Perspective on Pivotal Trial Evidence (I)

Trial Design Feature, Endpoints, Outcomes	FDA Perspective*	CMS Perspective*
Overall study design objectives	Maximize internal validity and patient safety. ("Efficacy")	Balance internal validity with generalizability to real-world patient populations and standards of practice for Medicare beneficiaries ("Effectiveness")
Treatment Indication	Protocol usually includes a precise definition of intended use	Must be an indication falling within statutory coverage as well as "medically necessary for treatment of illness or injury"
Study patient characteristics	Enrollment constrained by specific inclusion and exclusion criteria; patients with serious comorbid conditions are often excluded	Include patients who are representative of the Medicare population; these patients often have comorbid conditions)
Physician characteristics	Trial will "…restrict the use of the device to skilled surgeons trained in the proper technique to implant the device." (Text of an actual trial protocol)	Would probably prefer a range of settings and physician types to more closely mimic real world situation
Study comparator	As justified by intent of the trial: historical control, placebo, standard of care, sham treatment	Compare vs. community standard of treatment

FDA vs. CMS Perspective on Pivotal Trial Evidence (II)

Trial Design Feature, Endpoints, Outcomes	FDA Perspective*	CMS Perspective*
Course of treatment during the trial	Treatment administered per protocol with scheduled visits and procedures	Appropriate treatment, in accordance with guidelines and the standard of care
Study endpoint	FDA accepts intermediate endpoints clearly linked to the intervention; e.g., “obesity surgery results in significant weight loss”	CMS differentiates between intermediate endpoints and outcomes that describe patient welfare; e.g., “obesity surgery can achieve reduction in cardiovascular disease”
Duration of follow-up	Sufficient to evaluate specified endpoints, safety	Sufficient to establish a lasting impact on patient health and functional status as appropriate to the nature of the intervention
Incremental cost of treatment relative to standard of care	Not relevant	Clinical endpoints accepted by FDA such as hospital readmission have economic significance
Incremental cost-effectiveness relative to standard of care	Not relevant	Evidence to justify new codes, and payment, higher payment for existing code, or add-on payment

The challenge!

"Doing double duty" is a bit like having our cake and eating too!

We need to meet FDA requirements for internal validity…

…while addressing CMS desire for generalizability to the community standard of care in a Medicare population…

…and along the way, let's collect additional data on resource use and cost of treatment…

Implications for "Doing Double Duty"

- **FDA trial design requirements are the point of departure**

- **Availability of data to address the CMS stakeholder information needs may involve:**
  - leveraging trial design features and data elements required for FDA submission *or*
  - addition of trial components and data elements not directly relevant to FDA submission *or*
  - negotiation with FDA to establish trial design features that better address CMS requirements

Recommendations

Leveraging a Registration Study to Support CMS Coverage and Reimbursement

1. Planning is Critical

- **What value messages will be communicated to CMS?**
  - Cost savings?
  - Cost offsets?
  - Higher cost with better outcome?

- **What data will be needed to construct this message?**
  - In many cases, economic impact of the intervention is uncertain
  - Design the trial to explore various economic value propositions

2. Focus on Critical Protocol Issues

- **Comparator**
  - Historical control
  - Placebo
  - Standard of care
  - Sham treatment
- **Inclusion-exclusion criteria**
  - Include patients who “represent” Medicare population
  - What proportion of enrollment is adequate?
- **Endpoints**
  - Consider secondary endpoints specifically targeted to CMS issues
- **Duration of study treatment episode**
  - Sponsors typically want to keep this short and get to market
  - Consider a registry to extend the follow-up period

CMS Non-Coverage Decisions

Comparator

"The non-inferiority study that led to the FDA's approval (of Charité) was a comparison to fusion with a BAK cage, which has fallen out of favor.

Patient population

"The evidence is not adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP) and laparoscopic adjustable gastric banding (LAGB) are reasonable and necessary for Medicare beneficiaries who are 65 years of age or older"

3. Consider Patient-reported Outcomes

- For many medical devices, the primary benefit is improved quality of life rather than survival
- FDA/CDRH recognizes patient-reported outcomes as valid endpoints, and is applying increasingly rigorous review criteria to both protocols and submitted data
- CMS cares about the impact of treatment on beneficiary functional status, activities of daily living, quality of life, and QALYs

4. Design CRFs for "Double Duty" to Collect Economic Data

- **Many "clinical events" of interest to FDA (and well documented in CRFs) involve use of medical resources**
  - Study intervention
  - Adverse events
  - Unscheduled follow-up treatments including rescue therapy
- **Clinical events can be cross-walked to standard billing codes (DRG, CPT, APC)**
  - Standard Medicare payment rates can be applied to codes to estimate cost of treatment
- **Design CRF to facilitate this process**
  - Use standard terminology if possible (e.g., ICD9 dx/px, MedDRA,)
  - Ensure that required billing data elements are available (e.g., hospital admission CRF mimics UB-92)

5. Supplement Trial Results with Economic Modeling

- **Protocol-induced costs**
  - Model scenario where trial-mandated treatment costs are removed
- **Duration of follow-up**
  - Model various durations of treatment course, using other sources of data to justify persistence of treatment effects
- **Patient selection criteria**
  - Model sub-sets of the trial data
- **Device performance characteristics**
  - Model expected improvements such as increased battery life
- **Learning curves**
  - Model proficiency gains (e.g., decrease in OR time, infection rate, recovery time)

Summary

- Registration trials can do “double duty” by simultaneously generating evidence to support CMS coverage and payment decisions
- Inherent conflict in FDA’s focus on internal validity vs. CMS need to predict clinical, humanistic, and economic outcomes in the Medicare population
- Three principles of protocol/CRF design
  - Leverage data needed for FDA to document resource use
  - Supplement with additional data collection as needed for CMS
  - Try to select a comparator acceptable to both FDA and CMS
- Plan for additional evidence generation to meet CMS needs not addressed by the trial
  - Modeling
  - Registry studies